BSC 489 Independent Studies (3 Credit Hours) - Fall 2012
(Rudy Castillo, Sravan Vemuri, and Danyelle Butts)

Interferon Stimulated Genes and Cancer

Instructor: Dr. Venugopalan Cheriyath, STC 352, STC 353 & STC 332

Purpose: Gain a better understanding of interferons (IFN) and its target genes in cancer development and progression.

Specific study objectives for each student:
Rudi Castillo

1. Investigate the antitumor activity of IFNs in pancreatic cell carcinomas.
2. Gain a better understanding of cancer promoting activity of IFNs in pancreatic cell carcinomas.
3. Investigate the role of G1P3 in antagonizing IFN mediated apoptosis in pancreatic cell carcinomas.
4. Present research findings in Pathway Symposium in Fall-2012.

Sravan Vemuri

1. Perform multivariate analysis on ISGs with significant effect on breast cancer patient outcomes.
2. Investigate the effect of IFIT1 on breast cancer progression.
3. Present research findings in Pathway Symposium in Fall-2012.

Danyelle Butts

1. Investigate the effect of G1P3, one of the first discovered ISG, on actin organization.
2. Investigate the interaction between G1P3 and cytoskeleton system in breast carcinomas.
3. Present research finding in Pathway Symposium in Fall-2012.

Grading Scheme

Attendance and Participation	45 Points
Cell culture	15 points
Immunoblot analysis & Immunoprecipitation	15 points
Statistical Analysis	5 points

Presentation	10 points
Report	10 points

Requirements:

All students will be working under my direct supervision. Students are required to attend all lab meetings and attempt at least 10 hours of laboratory work per week. Depending on the experiments they may require to come to the everyday of the week including week ends.

Important References

1. Akiyama, T., Dass, C.R., and Choong, P.F. (2009). Bim-targeted cancer therapy: a link between drug action and underlying molecular changes. Mol Cancer Ther *8*, 3173-80.
2. Beere, H.M. (2005). Death versus survival: functional interaction between the apoptotic and stress-inducible heat shock protein pathways. J.Clin.Invest *115*, 2633-2639.
3. Bondar, V.M., and McConkey, D.J. (2002). Anoikis is regulated by BCL-2-independent pathways in human prostate carcinoma cells. Prostate *51*, 42-9.
4. Calogero, R.A., Cordero, F., Forni, G., and Cavallo, F. (2007). Inflammation and breast cancer. Inflammatory component of mammary carcinogenesis in ErbB2 transgenic mice. Breast Cancer Res *9*, 211.
5. Chen, Q., Gong, B., Mahmoud-Ahmed, A.S., Zhou, A., Hsi, E.D., Hussein, M., and Almasan, A. (2001). Apo2L/TRAIL and Bcl-2-related proteins regulate type I interferon-induced apoptosis in multiple myeloma. Blood *98*, 2183-92.
6. Cheriyath, V., Glaser, K.B., Waring, J.F., Baz, R., Hussein, M.A., and Borden, E.C. (2007). G1P3, an IFN-induced survival factor, antagonizes TRAIL-induced apoptosis in human myeloma cells. J Clin Invest *117*, 3107-17.
7. Cheriyath, V., Kuhns, M.A., Jacobs, B.S., Evangelista, P., Elson, P., Downs-Kelly, E., Tubbs, R., and Borden, E.C. (2011a). G1P3, an interferon- and estrogen-induced survival protein contributes to hyperplasia, tamoxifen resistance and poor outcomes in breast cancer. Oncogene.
8. Cheriyath, V., Leaman, D.W., and Borden, E.C. (2011b). Emerging roles of FAM14 family members (G1P3/ISG 6-16 and ISG12/IFI27) in innate immunity and cancer. J Interferon Cytokine Res *31*, 173-81.
9. Cuello, M.A., Nau, M., and Lipkowitz, S. (2002). Apoptosis and the treatment of breast cancer. Breast Dis *15*, 71-82.
10. Dawson, S.J., Makretsov, N., Blows, F.M., Driver, K.E., Provenzano, E., Le Quesne, J., Baglietto, L., Severi, G., Giles, G.G., and McLean, C.A., et al. (2010). BCL2 in breast cancer: a favourable prognostic marker across molecular subtypes and independent of adjuvant therapy received. Br J Cancer *103*, 668-75.
11. Debnath, J., Muthuswamy, S.K., and Brugge, J.S. (2003). Morphogenesis and oncogenesis of MCF-10A mammary epithelial acini grown in three-dimensional basement membrane cultures. Methods *30*, 256-268.

12. Ding, H.F., and Fisher, D.E. (2002). Induction of apoptosis in cancer: new therapeutic opportunities. Ann Med *34*, 451-69.
13. Eroles, P., Bosch, A., Bermejo, B., and Lluch, A. (2010). Mechanisms of resistance to hormonal treatment in breast cancer. Clin Transl Oncol *12*, 246-52.
14. Frisch, S.M., and Screaton, R.A. (2001). Anoikis mechanisms. Curr Opin Cell Biol *13*, 555-62.
15. Hardwick, J.M. (1998). Viral interference with apoptosis. Semin.Cell Dev.Biol *9*, 339-349.
16. Hebner, C., Weaver, V.M., and Debnath, J. (2008). Modeling morphogenesis and oncogenesis in three-dimensional breast epithelial cultures. Annu.Rev.Pathol *3*, 313-339.
17. Hur, J., Chesnes, J., Coser, K.R., Lee, R.S., Geck, P., Isselbacher, K.J., and Shioda, T. (2004). The Bik BH3-only protein is induced in estrogen-starved and antiestrogen-exposed breast cancer cells and provokes apoptosis. Proc Natl Acad Sci U S A *101*, 2351-6.
18. Mailleux, A.A., Overholtzer, M., Schmelzle, T., Bouillet, P., Strasser, A., and Brugge, J.S. (2007). BIM regulates apoptosis during mammary ductal morphogenesis, and its absence reveals alternative cell death mechanisms. Dev.Cell *12*, 221-234.